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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/831,805	05/10/2001	Henry Yuc	PF-0643 USN	9732

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EXAMINER

HADDAD, MAHER M

ART UNIT PAPER NUMBER

1644

DATE MAILED: 06/11/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/831,805

Applicant(s)

YUE ET AL.

Examiner

Maher M. Haddad

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 02 April 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 21-44 is/are pending in the application.
- 4a) Of the above claim(s) 23,25-31 and 34-44 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 21-22, 24 and 32-33 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

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RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 4/2/04, is acknowledged.
Discussed
2. Claims 21-44 are pending.
3. Claims 23, 25-31 and 34-44 stand withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to a nonelected invention.
4. Claims 21-22, 24 and 32-33 are under examination as they read on a purified polypeptide comprising SEQ ID NO: 6, fragments thereof and a composition thereof.
5. In view of Applicant response and the declarations of Dr. Rockett, Dr. Bedilion, Dr. Iyer filed on 4/2/04, only the following grounds of rejections are remained.
6. The following is a quotation of the first paragraph of 35 U.S.C. 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.
7. Claims 21-22, 24, and 32-33 stand rejected under 35 U.S.C. 112, first paragraph because the specification, while being enabling for the polypeptide comprising an amino acid sequence of SEQ ID NO:6 does not reasonably provide **enablement** for (a) any polypeptide comprising a "naturally occurring" amino acid sequence "at least 90% identical" to any amino acid sequence of SEQ ID NO:6, (b) any biologically active fragment of any polypeptide having any amino acid sequence of SEQ ID NO: 6, and (c) any immunogenic fragment of any polypeptide having any amino acid sequence of SEQ ID NO: 6 in claims 21-22 and 24; any composition comprising any polypeptide of and (b) or (c) mentioned above. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and or use the invention commensurate in scope with this claim for the same reasons set forth in the previous Office Action mailed 12/31/03.

Applicant's arguments, filed 4/2/04, have been fully considered, but have not been found persuasive.

Applicant submits that the specification discloses methods to make a polypeptide **having** any particular amino acid sequence (at page 25, lines 9-19). On the bases the specification discloses SEQ ID NO: 6, Applicant concluded that one skill in the art would be able to routinely obtain a "naturally occurring" amino acid sequence at least 90% identical to any amino acid sequence of SEQ ID NO: 6 including biologically active and immunogenic fragments of SEQ ID NO: 6.

Contrary to Applicant's assertions, the specification fails to provide sufficient guidance as to which core structure of SEQ ID NO: 6 is essential for maintain its activity and which changes

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can be made in the structure of SEQ ID NO: 6 and still maintained the same function. Furthermore, the term "comprising" is an open-ended and expands the "naturally occurring amino acid", "biologically active fragment" and "immunogenic fragment" of SEQ ID NO: 6 to include additional non disclosed amino acids.

Applicant submits in conjunction with case law that the specification discloses how to make the polypeptides of SEQ ID NO: 6, variants and biologically active and immunogenic fragments thereof.

However, it is recognized in the prior art that the function of a protein depends on the sequence of its amino acids in a certain pattern, conformation of the protein due to the amino acid sequence and the functional properties of the different parts of the protein. The specification does not teach which changes in the amino acid of SEQ ID NO:6 would not alter all the activities of the fragments. Therefore, the specification fails to provide sufficient guidance as to which core structure of SEQ ID NO: 6 is essential for maintain its inhibitory activity and which changes can be made in the structure of SEQ ID NO: 6 and still maintained the same function.

Applicant submits that predictability of other "naturally-occurring" variant polypeptides is not needed in order to make such polypeptides. That is, the claims define the variant polypeptides as "naturally occurring" and being at least 90% identical to the amino acid sequence of SEQ ID NO: 6. The existence of such variants is made by nature; and "naturally occurring" polypeptide variants occur in nature. The specification teaches how to find polynucleotide variants (See, e.g., page 40, lines 19-29) which can then be expressed to make polypeptide variants. The specification also teaches how to use antibodies to purify naturally occurring IGFAM-6 (See, e.g., page 54, lines 24-34). The scope of the polypeptide variants is described by the phrase "at least 90% identical to the full length of the sequence of SEQ m NO:6." The Specification describes how to use BLAST to determine whether a given sequence falls within the "at least 90% identical" scope (See, e.g., page 14, line 28 through page 15, line 22; page 48, lines 6-31). In addition, determination of percentage identity is well known in the art. Moreover, the "comprising" language used to define the variant polypeptides does not preclude the ability to make the claimed subject matter. The term "comprising" as used in the specification merely encompasses, for example, fusion proteins which contain the variant sequences (See, e.g., page 29, line 28 through page 30, line 11; page 52, lines 14-25). Methods for making fusion proteins are well known in the art.

However, there does not appear to be sufficient guidance in the specification as filed as to how the skilled artisan would make and use the various amino acids recited in the instant claims. A person of skill in the art would not know which sequences are essential, which sequences are non-essential, and what particular sequence lengths identify essential sequences. There is insufficient guidance to direct a person of skill in the art to select particular sequences or sequence lengths as essential for the polypeptide activity. Without detailed direction as to which amino acid sequences are essential to the function of the polypeptide, a person of skill in the art would not be able to determine without undue experimentation which of the plethora of amino acid sequences encompassed by the instant claims would share the ability to inhibit

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transmigration of monocytes across endothelial cell layers in vitro of the polypeptide of SEQ ID NO:6, other than the amino acid of SEQ ID NO:2.

Applicants submit that the specification fully enables the making of the claimed biologically active fragments of the SEQ ID NO:6 polypeptide. The polypeptide sequence of SEQ ID NO:6 is provided in the Sequence Listing. Possible amino acids and polypeptide fragments of SEQ ID NO:6 which are biologically active are taught in the Specification on page 60, Table 2, columns 3-5. Preparation of biologically active fragments is described in the Specification, e.g., at page 25, lines 6-23. Determinations of biological activity of IGFAM-6 and biologically active fragments thereof are taught in the Specification, e.g., page 52, line 26 through page 53, line 11. Applicant points to the specification which states that "biologically active" refers to a protein having structural, regulatory or biochemical functions of a naturally occurring molecule." (page 10 lines 18-19.) Applicant contends that prediction of biologically active fragments may be done using methods described in the specification, such as the use of PROFTI-ESCAN, BLIMPS, MOTYS, and PFAM software programs as well as the algorithms taught in Table 5, pages 71-72.

Again, Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions. Due to the large quantity of experimentation necessary to obtain "non-naturally-occurring" IGFAM-6 polypeptide variants, to generate the infinite number of derivatives recited in the claims (for at least 90% of SEQ ID NO:6 would be 31^{20} variants), and to determine the specific activity of the infinite variants, the lack of direction/guidance presented in the specification regarding the same, the absence of working examples directed to the same, the complex nature of the invention, the state of the prior art which establishes that biological activity cannot be predicted based on structural similarity, and the breadth of the claims which embrace a broad class of structural variants, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Applicant submits that the specification fully enables the making of the claimed immunogenic fragments of the SEQ m NO:6 polypeptide. Applicant submits that the polypeptide sequence of SEQ m NO:6 is provided in the Sequence Listing. Possible polynucleotide fragments of SEQ ID NO:25 which encode potential immunogenic fragments of SEQ m NO:6 are taught in the Specification on page 64, Table 3, column 2. Applicant submits that preparation of immunogenic fragments is described in the specification, e.g., at page 21, lines 22-26 and page 54, lines 8-23. Applicant points to the specification which states that "immunologically active" refers to the capability of the natural, recombinant, or synthetic IGFAM, or of any oligopeptide thereof, to induce a specific immune response in appropriate animals or cells and to bind with specific antibodies." (page 10 lines 19-21.) The terms "immunologically active" and "immunogenic" are interchangeable. Prediction of immunogenic fragments may be done using methods described in the Specification, such as the use of DNASTAR software, as well as choosing possible epitopes near the C-terminus or in hydrophilic regions, e.g., on page 54, lines 8-23. The ability of a given fragment to induce a specific immune response in appropriate

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animals or cells and to bind with specific antibodies are tests for whether the fragment is "immunogenic" (See, e.g., page 10 lines 19-21, page 12, lines 28-34, page 32, line 32 through page 33, line 11, and page 54, lines 8-23). Applicant submits that the tests of fragments by these methods are routine practices in the art and, hence, do not require undue experimentation (In re Wands (858 F.2d 731, 8 USPQZd 1400) Fed. Cir. 1988); the specification provides a test for antibody binding (See, e.g., at page 34, lines 3-9).

However, the specification does not appear to have provided sufficient guidance as to which subsequences of SEQ ID NO:6 would share the ability to inhibit transmigration of monocytes across endothelial cell layers in vitro. Neither does the specification appear to have provided any working examples of any functional subsequences "i.e., immunogenic fragments". Thus it would require undue experimentation of the skilled artisan to determine which subsequences of SEQ ID NO:6 would have the function of the full length molecule.

Applicant argues that he does not need to establish the three-dimensional structure of each variant will be the same as that of the protein encoded by SEQ ID NO:6 in order to enable the claimed variants. One of ordinary skill would be able to use the claimed polypeptide variants in toxicology studies regardless of their three-dimensional structure.

However, mere presentation of SEQ ID NO:6, does not mean that the polypeptide variant is an appropriate target for toxicology testing. Cells and tissues can express many polypeptides, such as constitutively expressed polypeptides, which are not appropriate toxicology targets. Further, the particulars of toxicology testing with the claimed polypeptide variants and fragments are not disclosed in the instant specification.

Applicant asserts that the claims at issue do not describe a genus which is highly variant, but rather a genus that is narrow in scope. Applicant points to Brenner et al. to support their position. Brenner et al. have determined that 30% identity is a reliable threshold for establishing evolutionary homology between two sequences aligned over at least 150 residues. (Brenner et al., pages 6073 and 6076.) Furthermore, local identity is particularly important in this case for assessing the significance of the alignments, as Brenner et al. further report that $\geq 40\%$ identity over at least 70 residues is reliable in signifying homology between proteins. (Brenner et al., page 6076.)

However, Applicant has not provided evidence to demonstrate that the skilled artisan would be able to envision the detailed structure of the infinite number of polypeptides recited in the claims. The specification and claims do not indicate what characteristics are shared by members of the genus. The scope of the claims include numerous structural variants and the genus is highly variant because a significant number of structural differences between genus members is permitted. However, the specification and claims do not provide any guidance as to what changes should be made and structural features that distinguish polypeptides in the same genus from others in the protein class are absent from the specification. The specification fails to

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disclose the common characteristics that identify members of the genus, and because the genus is highly variant, SEQ ID NO: 6 are insufficient to describe the genus.

Consequently, without additional guidance in the specification, and the dearth of information in the art, for one of skill in the art to practice the invention as claimed, would require experimentation that is excessive and undue. The amount of guidance or direction needed to enable an invention is inversely related to the mount of knowledge in the state of the art as well as the predictability in the art (In re Fisher, 427 F.2d 833, 839, 166 USPQ 18,24 (CCPA 1970)).

8. Claims 21-22, 24, and 32-33 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is in possession of SEQ ID NO: 6.

Applicant is not in possession of (a) any polypeptide comprising a “naturally occurring” amino acid sequence at least 90% identical to any amino acid sequence of SEQ ID NO:6, (b) any biologically active fragment of any polypeptide having any amino acid sequence of SEQ ID NO: 6, or (c) any immunogenic fragment of any polypeptide having any amino acid sequence of SEQ ID NO: 6 in claims 21-22 and 24; any composition comprising any polypeptide of and (b) or (c) mentioned above for the same reasons set forth in the previous Office Action mailed 12/31/03.

Applicant's arguments, filed 4/2/04, have been fully considered, but have not been found persuasive.

A. The specification allegedly provides an adequate written description of the claimed “variants” of SEQ ID NO: [1] 6

Applicant argues that the subject matter encompassed by the claims is disclosed by the specification or is conventional or well known to one skilled in the art. Applicant contends that polypeptide variants having at least 90% identity to SEQ ID NO:6 are described at page 22, lines 2-5 of the specification. Applicant also submits that the specification at page 8, lines 21-23 defines “IGFAM” as “the amino acid sequences of substantially purified IGFAM obtained from any species, particularly a mammalian species, including bovine, ovine, porcine, murine, equine, and human, and from any source, whether natural, synthetic, semi-synthetic, or recombinant.” Applicant asserts that one skill in the art would be able to routinely recognize and obtain “a naturally occurring amino acid sequence having at least 90% sequence identity to the SEQ ID NO:6 using hybridization and/or PCR.

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However, to satisfy the written-description requirement, the specification must describe every element of the claimed invention in sufficient detail so that one of ordinary skill in the art would recognize that the inventor possessed the claimed invention at the time of filing. *Vas-Cath*, 935 F.3d at 1563. The written-description requirement can be satisfied “by describing the invention, with all its claimed limitations, not that which makes it obvious,” and by using “such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention.” *Lockwood*, 107 F.3d at 1572. As for the recitation of “a naturally occurring amino acid sequence having at least 90% sequence identity to amino acid sequence of SEQ ID NO:6”. The court said that “an adequate written description of a DNA ... ‘requires a precise definition, such as by structure, formula, chemical name, or physical properties.’ Not a mere wish or plan for obtaining the claimed chemical invention.” *Eli Lilly*, 119 F.3d at 1566 (quoting *Fiers*, 984 F.2d at 1171). The Specification, fails to provide working examples of any variants or fragments. The specification only discloses SEQ ID NO: 6, none of the variants were provided, nor is there any guidance as to which should be used. The court stated that “an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it, what is required is a description of the DNA itself.” *Fiers* 984 F.2d at 1170.

1. The present claims allegedly define the claimed genus through the recitation of chemical structure.

Applicant submits that the polypeptide in the instant application define SEQ ID NO: 6 in terms of chemical structure rather than in terms of functional characteristics. Applicant indicates that in the present claims, there is no reliance on a description of functional characteristics of the polypeptides recited by the claims. Appellant contends that if such functional recitations were included in the claims, it would add to the structural characterization of the recited polypeptides. Appellant argues that by failing to base its written description inquiry “on whatever is now claimed”, the examiner failed to provide an adequate analysis of the present claims and how they differ from those found not to satisfy the written description requirement in *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) and *Regents of the University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

However, Applicant has not provided evidence to demonstrate that the skilled artisan would be able to envision the detailed structure of the infinite number of polypeptides recited in the claims. The description of one IGFAM-6 polypeptide encoded by SEQ ID NO:25 in the specification of the instant application is not a representative number of embodiments to support the description of an entire genus of functionally equivalent polypeptides which incorporate all mutants, derivatives, variants and fragments having at least 90% identity to the amino acid sequences of SEQ ID NO: 6. Therefore, only an isolated polypeptide of sequence of SEQ ID NO: 6, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Further, the “naturally occurring” language in the claims is analogous to the claims found in *Lilly and Fiers* because the claimed polypeptides are defined only by their homology to SEQ ID NO:6, which is insufficient to satisfy 112(1) since “a mere wish or plan” for obtaining an up to 10% variation in SEQ ID NO: 6 is not enough to comply with 112(1). Furthermore,

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there is no described or art-recognized correlation or relationship between the structure of the invention, the IGFAM-6 protein and its function, the feature deemed essential to the instant invention. Therefore, one of skill in the art would not envisage, based on the instant disclosure, the claimed genus of fragments and variants, wherein the variant has at least 90% sequence identity of SEQ ID NO: 6.

2. The present claims do not defined a genus which is “highly variant”.

Applicant argues that the claims at issue do not describe a genus which could be characterized as “highly variant” with respect to the “claimed genus of fragments and polypeptide that have at least 90% sequence identity of SEQ ID NO:6”.

Again. Applicant has not provided evidence to demonstrate that the skilled artisan would be able to envision the detailed structure of the infinite number of polypeptides recited in the claims. The specification and claims do not indicate what characteristics are shared by members of the genus. The scope of the claims include numerous structural variants and the genus is highly variant because a significant number of structural differences between genus members is permitted. However, the specification and claims do not provide any guidance as to what changes should be made and structural features that distinguish polypeptides in the same genus from others in the protein class are absent from the specification. The specification fails to disclose the common characteristics that identify members of the genus, and because the genus is highly variant, SEQ ID NO: 6 are insufficient to describe the genus.

3. IGFAM proteins contain Ig domains which are known to function in DNA binding.

Applicants submit that they have adequately described the claimed invention in terms of a method of its making together with providing both structural and functional characteristics and have provided evidence of a correlation between structure and function. Applicant submits that conventional methods for making the claimed polypeptide are described at page 25, lines 6-14 of the specification. Applicant further submits that the specification identifies the presence of Ig domains within SEQ ID NO:6. Applicants submit that they have provided an art recognized correlation between the Ig domain, a structural domain within the claimed invention, and the function of the Ig domain within Jam and so too, more likely than not, the Ig domain of IGFAM-6 functions in the control of monocyte migration across epithelium or endothelium.

However Applicant has not provide an amino acid variants that one skilled in the art would know would identify their polynucleotides. The specification does not disclose any representative number of a species of the amino acid sequence of SEQ ID NO:6, therefore, one skill in the art cannot identify variants of SEQ ID NO:6. Appellant is not in possession of a genus (see MPEP 2163 II A.3 (a)ii)).

4. The state of the art at the time of the present invention is allegedly further advanced than at the time of the Lilly and Fiers applications.

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Applicant contends that much has happened in the development of recombinant DNA technology in the 17 or more years from the time of filing of the applications involved in Lilly and Fiers and the present application. Applicant indicates that, for example, PCR, highly efficient cloning and DNA sequencing technology has been developed. Applicant asserts that with the current advances, one of skill in the art would recognize that, given the sequence information of SEQ ID NO: 6 and the additional extensive detail provided by the application, the present inventors were in possession of the polypeptide variants recited by the claims at the time of filing of this application.

However, the broad brush discussion of making and screening for allelic variants does not constitute a disclosure of a representative number of members. No such variants were made or shown to have activity. Only the polypeptides IGFAM-6 of SEQ ID NO: 6 is disclosed. The specification's general discussion of making and screening for variants is not equivalent to making such variants. Such does not constitute an adequate written description for the claimed variants. Further, in order to satisfy the U.S.C 112, 1st paragraph, the specification has to teach how to make and use the invention, not how to identify the invention. Until the time when at least 90% sequence identity to the claimed claimed polypeptide are found, then one skill in the art can make them. Undue experimentation would be required of the skilled artisan to obtain "naturally occurring" IGFAM variants and fragments and determine their specific activity.

9. No claim is allowed.

10. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad whose telephone number is (571) 272-0845. The examiner can normally be reached Monday through Friday from 7:30 am to 4:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax number for the organization where this application or proceeding is assigned is 703-872-9306.


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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Maher Haddad, Ph.D.

Patent Examiner

June 7, 2004


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